Report on Project 2.2
Prepared for April 1998 meeting of the Joint Scientific Review Group (SRG)
March 1998

Title of Project: Estimation of Risk of Stochastic (Cancer) Effects of Occupational Radiation Exposure

Principal Investigators: Nina A. Koshurnikova, Branch 1 of the Biophysics Institute, Ozersk and Ethel S. Gilbert, National Cancer Institute, Bethesda MD

Background.

Currently radiation risk estimates for carcinogenic effects are based on epidemiologic studies of Japanese A-bomb survivors, supplemented by studies of persons who received radiation therapy. Despite the large amount of data accumulated, questions remain regarding the appropriateness of using radiation risk estimates obtained from a single exposure at high dose rates (as in the A-bomb survivor studies) for other practically important exposure scenarios, including protracted exposures and exposure from internally deposited radio nuclides. Studies of externally exposed workers in the United States, United Kingdom, Canada and other countries provide a direct evaluation of risks from protracted exposure to external radiation, but the relatively low doses received by most workers limits power for studying the possible modifying effects of exposure protraction, and studies conducted thus far have shown consistency both with no risk and risks that are somewhat larger than those obtained from high dose studies. Also, because most of the exposure was to males, almost no information is available on radiation risks in female workers. Studies of US workers can provide only very limited information on plutonium-related health effect since only about 50 of these workers had plutonium body burdens exceeding 1,480 Bq, the lifetime maximum permissible body burden guideline used in the US during most of the follow-up period.

Studies of workers at the Mayak nuclear facility, located in the Chelyabinsk region of the Russian Federation, can fill important gaps in our knowledge of radiation risks by providing information on protracted external exposure at high doses, on occupational exposure in females, and on exposure from internally deposited plutonium. The Mayak facility, which began operations in 1948 and which is managed by the Mayak Production Association (PA), has nuclear reactors, a radiochemical plant, and a plutonium production facility. During the first decade of Mayak's operation, workers at the plants were exposed to doses of external gamma radiation that were substantially higher than current occupational dose limits, and were also exposed to inhaled plutonium at levels much higher than those considered permissible today. Film badge dosimetry data for the Mayak cohort are available at the Radiation Safety Service of the Mayak PA. Data on levels of plutonium content in excreta, accumulated since 1970 from periodic biophysical examinations of workers at the facility, are available at Branch 1 of the Biophysics Institute (FIB-1), and have been used to develop estimates of dose to the lung and other organs for about 30% of workers with a high probability of exposure.

About ten years ago, Dr. Koshurnikova and colleagues at FIB-1 began to create the Mayak Worker Registry. Information was extracted from several sources and much of it has been computerized. Three computerized registries (nuclear reactors, radiochemical plant, plutonium production facility) contain annual and cumulative gamma doses, plutonium body burdens and internal doses to the main organs of plutonium deposition (lung, liver and bone), date and place of birth, current and past names, current place of residence, vital status, date and causes of death.

Vital status has been determined primarily through the use of the Ozersk address bureau, and, for non-residents, by making inquiries at address bureaus in places where subjects have subsequently resided. Data on date and cause of death are obtained from several sources depending on where the death occurred. Vital status is known for about 89% of all workers, but this percentage is 85% for persons who began working between 1948-53.

The Mayak Worker Registry currently includes about 19,000 persons. About 14,000 of these workers have known vital status and film badge dosimetry data, and more than 4,000 have measured plutonium body burdens. About 4,000 persons have died, 1,000 of them from cancer. The average external gamma-dose for workers included in the registry is 0.88 Gy: 0.66 Gy for the reactor plant workers, 1.22 Gy for the radiochemical plant workers, and 0.44 Gy for the plutonium production plant workers. These radiation doses decreased significantly with time with average external doses of 1.57, 0.57, 0.27 and 0.15 Gy for workers hired in the respective time periods 1948-53, 1954-58, 1959-63, and 1964-72. The average value of the equivalent dose to the lung for all workers with plutonium body burdens above the detection limit is 7.06 Sv: 4.09 Sv for the radiochemical plant workers, and 10.71 Sv for the plutonium production plant workers.

Project 2.2 includes 5 tasks, which are briefly described below.

Task 1: Improvement of the computer database. Data on where workers were employed (reactor, radio-chemical, and plutonium production) during any given time period will be improved. In addition, a comprehensive set of logical checks will be developed, documented, and performed; and any identified discrepancies will be resolved.

At the present time, the computer database is organized so that workers are assigned to one of three registries according to the plant they worked in: reactors, radio-chemical plant, or plutonium production plant. Subjects who were employed in more than one plant were assigned to the most dangerous plant even though, in some cases, they may have spent a substantial portion of their work history in other plants. For this assignment, the plutonium production plant is considered the most dangerous, and the reactors the least dangerous.

Task 1 is aimed at developing a database that includes all workers, and that provides data on which of the three plants workers were employed during any given time period. This information is available but has not been fully computerized. Such information is

important for performing appropriate epidemiologic analyses, and also for evaluating potential biases in dose estimates.

Task 2: Update of vital status data. Data on vital status and cause of death will be updated to extend to the end of 1996.

Task 3: Development of an adequate control group. A control group will be developed from unmonitored workers and from workers at the auxiliary plants of Mayak.

Preliminary analyses of Mayak worker data have been based on comparisons with national vital statistics, but the appropriateness of such comparisons is questionable given concerns related to the "healthy worker effect". Also, relevant national statistics for the USSR are not available for all disease categories of interest, and are often limited to recent calendar years and/or broad age categories. Furthermore, because the assignment of cause of death in Mayak workers has often made use of autopsy data and medical records, this information may not be comparable to that used in national statistics. It is noted that work conducted under the NCI contract has explored methods for adjusting available vital statistics based on the assumption that the ratios of rates for different ages remain constant over time, and has also compared causes of deaths assigned by different methods.

Studies of workers in the U.S., U.K., and Canada have relied primarily on internal comparisons by level of radiation dose. This approach has worked well because these studies have included large numbers of workers with little or no occupational exposure, and these workers have served to "anchor" the dose-response function, leading to more stable estimates of risk than would have been possible without such workers. By contrast, most monitored workers employed in the main Mayak facilities received substantial doses in the early period of Mayak operations making it difficult to conduct reliable internally based dose-response analyses. For example, among reactor workers who began working in 1948-1958, only 551 (of a total of 2413) had never received an annual dose exceeding 50 mGy. Use of workers in the radiochemical and plutonium production plants as controls is probably not reasonable because of the possibility of unmeasured plutonium exposure, since routine plutonium monitoring did not begin until 1970.

Task 4: Conduct dose-response analyses to evaluate risks of lung, liver and bone cancer resulting from plutonium exposure. Under the project currently being funded by the NCI, dose-response analyses based on currently available data on external doses are being conducted. Project 2.2 will expand these analyses to include analyses of lung, bone, and liver cancer (sites where internal exposure to plutonium contributes substantially to dose) based on estimated doses from both external and internal sources. These analyses would make use of the best available dosimetry data.

Task 5: Comparison of the results of analyses conducted under 2.2 with results from studies in the United States. Data on the effects of plutonium in U.S. workers are limited because of the generally small exposures and small sample sizes. Nevertheless, results from the Mayak cohort will be compared with available published results from U.S. studies.

Progress and Accomplishments. This covers the period from April 1, 1997, when the project first received USDOE support. No work on Tasks 4 and 5 was proposed for the first year, and thus the material below includes only Tasks 1, 2, and 3.

Task 1. Computer software has been developed that will allow entering the place of employment for each year that an external radiation dose was recorded. Similar software is being developed for periods of employment when external radiation dose was not received. Also, the estimation of dose from internal exposure to plutonium requires data on workers' moves between plants and even between different workplaces within plants. This information is available from the Biophysics laboratory, responsible for evaluating plutonium exposure. Scientists responsible for the epidemiologic studies collaborated in developing and verifying this information, which will be incorporated into the epidemiologic data base.

In addition, a system of logical checks has been established, including checks for discrepancies in age, cohort, year of hire, external doses, plutonium body burden and vital status. Instances where discrepancies were identified are being checked against source records (paper cards), but these checks are not yet complete. A document will be prepared that describes in detail the logical checks that were made, their results, the results of checks of identified discrepancies against source records, and any changes were made as a result of this process. It is expected that this document will be completed by September 1998. Table 1 provides preliminary data on the checks that are being made and the discrepancies that have been identified.

Task 2. Work on updating of vital status included the following. The exact birth date (including month and day of birth) was assigned to 159 subjects, date and cause of death information was obtained for 265 subjects, cause of death codes were corrected for 44 subjects, and vital status information was modified for 17 subjects (of the 17, vital status changed from unknown to known for 13 persons, and changed from known to unknown for 4 persons.). As of Sept. 1, 1997, the registry includes 18,870 subjects, and vital status is known for 85% on this group.

Task 3. Substantial work relevant to Task 3 has been completed. The two major sources of controls are unmonitored workers (not monitored for external radiation) who worked at the main plants and who are currently included in the Mayak Worker Registry, and auxiliary plant workers, who worked at auxiliary plants and departments of Mayak and who are not currently included in the registry. Because these workers may have visited the main plants and been exposed without adequate monitoring, available records need to be reviewed carefully.

Unmonitored workers. Data on 1,469 workers who were hired at the main "Mayak" PA plants in the period 1948-58 and who were not monitored for external radiation exposure were reviewed. Of these, 903 workers were determined to be potential controls in that they did not have evidence of having received external or internal exposure. This conclusion was based on the fact that their occupational histories indicated that they had worked in places where it would not be possible to have received such exposure. Before these 903 potential controls can definitely be used as a control group, a further more detailed investigation of their occupational histories is necessary. Table 2 summarizes the status of work to identify unmonitored workers who are suitable for use as controls.

Auxiliary workers. Workers in two auxiliary departments are being evaluated as potential controls. To date, the most extensive work has been conducted on workers at the mechanical repair plant. However, work has been initiated on workers at the water preparation plan (about half the records have been copied.)

The mechanical repair plant is located not at the "Mayak" site but inside the town. Some of the plant's personnel never visit the "Mayak" site, but others work in overhaul teams and thus are located permanently at the site, undergoing considerable levels of occupational exposure. In addition, there are a number of mechanical repair plant workers who worked previously at the main plants of "Mayak" PA or who moved there after work at the at the mechanical plant.

Personnel department information was reviewed on all people who were hired at the mechanical repair plant during the period 1948-1996. The status of this review is shown in Table 3. It can be seen that there is now information on 1,322 potential controls from the mechanical repair plant who were hired before 1973. For these workers, dose information in the "Mayak" PA radiation safety service will be checked. Work to determine the vital status of the group has been initiated. About half either remain in Ozersk or died in Ozersk, and efforts to determine vital status for those who left Ozersk are underway.

Questions and potential problems (to serve as the basis of the panel discussions).

Choice and use of various control groups.
How should various internal control groups be evaluated?
What controls are most suitable for evaluating the effects of external exposure?
What controls are most suitable for evaluating the effects of internal exposure?

How can external rates be improved or better utilized?

Would it be appropriate to use rates from the Baltic countries or from Belarus or any of the other Eastern Bloc countries?

Could we compare the few existing national Russian statistics to those from these other countries to see which country might be most similar?

How can available external rates best be used to evaluate the completeness of mortality ascertainment?

Dosimetry

Currently available dose estimates must be regarded as preliminary. While it is hoped that improved dosimetry will be developed, revised dose estimates are not likely to be available for a few years. What should be our approach to conducting analyses and publishing results and risk estimates based on dose estimates that are likely to be revised in the future?

Table 1. Logical checks and number of Mayak workers identified with various discrepancies. (This table is not yet complete, but is included to give a general sense of the edits that are being conducted, and the kinds of discrepancies that are being identified.)

Logical check discrepancy		Number of workers with
1.	Age at hire at a Mayak facility is less than 18.	957
2.	Age at hire at a Mayak main plant is less than 18. (For 1. and 2., initial checks indicate that in many cases, workers were initially hired before age 18 but then went into the military service and returned later to work at Mayak.)	670
3.	Date of hire is before 1948 or after 1972. (Most of these were workers hired in 1946 and 1947 before the first reactor began operations.)	685
4.	Age at hire at a Mayak facility is over age 60. (These were all found to agree with source records.)	11
5.	Date of hire at main plant is earlier than date of hire at Mayak.	0
6.	Date of discharge from Mayak is earlier than date of discharge from main plant.	1
7.	Discrepancy between cohort identification number and year of first inclusion in cohort (Cohort identification numbers assign workers to the groups 1948-53, 1954-58, 1959-63, 1964-72, 1972-82.)	355
8.	Year of first inclusion in cohort is less than year of hire at Mayak.	1
9.	Died before age 18	2
10.	Has data on plutonium body burden but no of indication biophysical examination data (These are instances where there is an indication of monitoring for plutonium, but where adequate data for evaluating this exposure may not be available. This could occur for persons examined before regular examinations were initiated in 1970.)	165
11.	Has biophysical examination data but no data on plutonium body burden	2
12.	Radiation exposure data under the age of 18.	175
13.	Radiation exposure data before employment at Mayak	9
14.	Total external dose is not equal to the sum of doses by year	0
15.	Number of years of radiation exposure is not equal to number of annual dose records	0
16.	Radiation exposure after termination of employment at Mayak (In many cases, this was a matter of radiation exposure being recorded a bit late, for example, in January for a person terminating in December. Occupational and radiation exposure histories are being checked for workers with larger discrepancies.	887
17.	Cause of death was not found in ICD-9 dictionary	31

Table 2. Number of unmonitored workers hired 1948-58 by plant and status as potential controls.

	Plant			
Radio-	Plutonium			
	Reactor	chemical	production	Total
Potential controls	267 (62%)	127 (51%)	509 (65%)	903 (61%)
Total for whom records were reviewed	431	249	789	1469

Table 3. Number of mechanical repair plant workers by year of hire and status as potential controls

	Year of hire*		
	1948-58	1959-72	Total
Potential controls	627 (67%)	695 (63%)	1,322 (65%)
Not suitable as potential controls	303 (33%)	412 (37%)	715 (35%)
Worked in overhaul teams	41	258	299
Also worked in main plants	262	154	416
Total	930	1,107	2,037

*An additional 818 workers were hired in the period 1973-1996, but these workers are not being investigated.